

WHAT IS CLAIMED IS:

1 1. A method of treating a subject with cancer by administration of a metal
2 chelate, said method comprising the steps of:

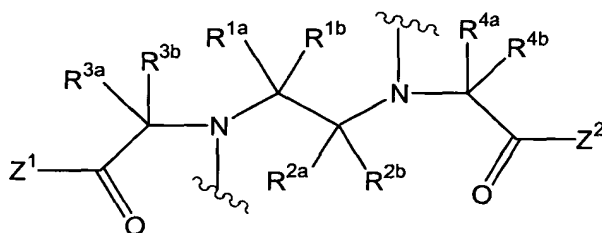
3 (a) administering to said subject an antibody comprising an antigen
4 recognition domain that recognizes a macrocyclic metal chelate, wherein said antibody
5 comprises a targeting moiety that binds specifically to a cell by binding with a member
6 selected cell surface receptors and cell surface antigens, thereby forming a cell-antibody
7 complex; and

8 (b) administering to said subject said metal chelate, thereby specifically
9 binding said compound to antibody to form a cell-antibody-metal chelate complex.

1 2. The method of claim 1, wherein said metal chelate comprises four
2 nitrogen atoms.

1 3. The method of claim 2, wherein at least two of said nitrogen atoms are
2 covalently linked to a substituted or unsubstituted ethyl bridge.

1 4. The method of claim 2, wherein said metal chelate comprises the
2 subunit:



3
4 wherein

5 Z¹ and Z² are members independently selected from OR and NR³R⁴

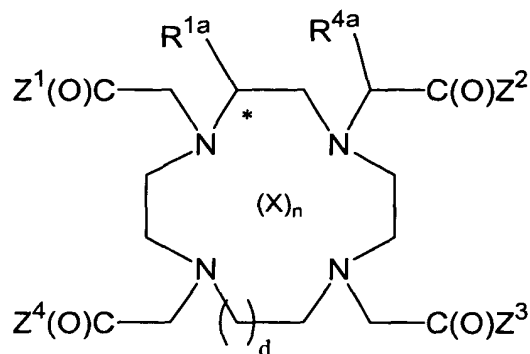
6 in which

7 R³ and R⁴ are members independently selected from H, substituted or
8 unsubstituted alkyl and substituted or unsubstituted heteroalkyl;

9 R^{1a}, R^{1b}, R^{2a}, R^{2b}, R^{3a}, R^{3b}, R^{4a} and R^{4b} are members independently selected
10 from H, substituted or unsubstituted alkyl, substituted or unsubstituted
11 heteroalkyl, substituted or unsubstituted aryl and linker moieties.

5. The method of claim 1, wherein said chelate is a member selected from substituted or unsubstituted DOTA and substituted or unsubstituted TETA.

6. The method of claim 4, wherein said chelate has the formula:



wherein

Z^1 , Z^2 , Z^3 and Z^4 are members independently selected from OR^1 and NR^1R^2

in which

R^1 and R^2 are members independently selected from H, substituted or unsubstituted alkyl and substituted or unsubstituted heteroalkyl;

X is a member selected from a lanthanide, an actinide, an alkaline earth metal, a group IIb transition metal, or a metal;

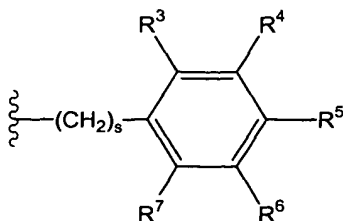
n is 0 or 1; and

d is 1 or 2.

7. The method of claim 1, wherein said macrocyclic metal chelate comprises a reactive functional group.

8. The method of claim 5, wherein the carbon atom marked * is of S configuration.

9. The method of claim 1, comprising a moiety having the formula:



wherein

R^3, R^4, R^5, R^6 and R^7 are members independently selected from H, halogen,
 NO_2 , CN, X^1R^8 , NR^9R^{10} , and $C(X^2)R^{11}$

wherein

X^1 is a member selected from O, NH and S;

R^8 and R^9 are members independently selected from H, substituted or
unsubstituted alkyl, substituted or unsubstituted heteroalkyl and
 $C(Z^3)R^{12}$

wherein

X^3 is a member selected from O, S and NH;

R^{12} is a member selected from substituted or unsubstituted
alkyl, substituted or unsubstituted heteroalkyl and OR^{13}

wherein

R^{13} is a member selected from substituted or
unsubstituted alkyl, substituted or unsubstituted
heteroalkyl, substituted or unsubstituted aryl and
substituted or unsubstituted heteroaryl;

R^{10} is a member selected from H, substituted or unsubstituted alkyl,
substituted or unsubstituted heteroalkyl and OH,

and R^9 and R^{10} , taken together are optionally ($=C=S$);

X^2 is a member selected from O, S and NH; and

R^{11} is a member selected from H, halogen, substituted or unsubstituted
alkyl, substituted or unsubstituted heteroalkyl, OR^{14} , $NR^{15}R^{16}$

wherein

R^{14} is a member selected from H, substituted or unsubstituted
alkyl, substituted or unsubstituted heteroalkyl, and
 $C(O)R^{17}$

wherein

R^{17} is a member selected from substituted or
unsubstituted alkyl and substituted or unsubstituted
heteroalkyl; and

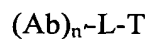
R^{15} and R^{16} are members independently selected from H,
substituted or unsubstituted alkyl and substituted or
unsubstituted heteroalkyl.

- 1 10. The method of claim 1, wherein said targeting moiety binds
2 specifically to a cell surface protein.
- 1 11. The method of claim 1, wherein the targeting moiety is covalently
2 attached to said antibody.
- 1 12. The method of claim 10, wherein the targeting moiety is an antibody.
- 1 13. The method of claim 11, wherein the targeting moiety specifically
2 binds to a protein on a cancer cell.
- 1 14. The method of claim 1, wherein the subject is a mammal.
- 1 15. The method of claim 1, wherein the mammal is a human.
- 1 16. A method of *in vivo* imaging, said method comprising the steps of :
2 (a) administering to a subject an antibody comprising an antigen recognition
3 domain that recognizes a macrocyclic metal chelate, wherein said antibody comprises a
4 recognition moiety that binds specifically to a cell, thereby forming a cell-antibody complex;
5 (c) administering to said subject said metal chelate, thereby specifically
6 binding said compound to said antibody to form a cell-antibody-metal chelate complex; and
7 (d) detecting said cell-antibody-metal chelate complex.
- 1 17. The method of claim 16, wherein said metal chelate comprises four
2 nitrogen atoms
- 1 18. The method of claim 16, wherein the step of detecting is by positron
2 emission tomography.
- 1 19. The method of claim 16, wherein the step of detecting is by magnetic
2 resonance imaging.
- 1 20. The method of claim 16, wherein the step of detecting is by detection
2 of lanthanide luminescence.
- 1 21. The method of claim 16, further comprising, between steps (a) and (b),
2 administering a clearing agent to said subject.

22. The method of claim 16, wherein the subject is a mammal.

23. The method of claim 22, wherein the mammal is a human.

24. A composition having the structure:



wherein,

n' is an integer from 1-10;

Ab represents an antibody comprising an antigen recognition domain that recognizes a macrocyclic metal chelate;

L is a chemical bond or linking group that may contain one or more functional groups; and

T is said targeting moiety.

25. The composition of claim 24, wherein said metal chelate comprises four nitrogen atoms.

26. The composition of claim 24, wherein said targeting moiety is an antibody that binds specifically to a cell surface antigen.

27. A pharmaceutical composition comprising the composition of claim 24, and a pharmaceutically acceptable carrier.